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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,581	09/29/2003	Yuuki Tsutsui	019941-001810US	5398

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/674,581	TSUTSUI ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 21-27* is/are pending in the application.

4a) Of the above claim(s) *21-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-19 in the reply filed on 4/13/2006 is acknowledged. The traversal is on the ground(s) that there would be no undue search burden to search the claims of group I, drawn to a vaccine composition and a mucosal adjuvant, and group III, drawn to methods for inducing mucosal immunity. This is not found persuasive because, as stated in the restriction requirement mailed on 3/7/2006, groups I and III are related as product and process of use. Thus, the groups represent distinct inventions, and searching both groups would constitute an undue search burden for the Office.

Group II (claim 19) was cancelled by the Applicant in the response received on 4/13/2006. Therefore claims 1-19 and 21-27 are currently pending, and claims 1-19 are the subject of this Office Action.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement received on 4/13/2006 has been fully considered by the Examiner.

Claim Objections

1. The Examiner suggests that the language of claim 7 can be improved by amending the phrase "this mucosal adjuvant" to "said mucosal adjuvant". Furthermore, it is suggested that the phrase "and with which mucosal administration" be amended to read "and wherein mucosal administration". Similarly, it is suggested that claim 13, which recites "with which said mucosal adjuvant comprises" be amended to read "wherein said mucosal adjuvant comprises", and claim 18, which recites "with which administration of the interferon" be amended to read "wherein administration of the interferon".

2. Claims 8 and 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically, claim 8 is drawn to a mucosal adjuvant according to claim 7, wherein the adjuvant is selected from natural or recombinant interferon (IFN)-α. Claim 7 recites a mucosal adjuvant comprised of IFN-α. Because the specification, on p. 6-7 defines IFN-α as any IFN-α polypeptide, from any source, and including natural and recombinant IFN-α, claim 7 is also drawn to natural and recombinant IFN-α, and therefore, claim 8 does not further limit the subject matter of claim 7. Claim 14 ultimately depends from claim 7, and for the same reasons as claim 8, does not further limit the subject matter of claim 7.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mucosal adjuvant comprised of murine IFN-α, as described in Examples 1-2, does not reasonably provide enablement for a mucosal adjuvant comprised of any other IFN-α. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The breadth of the claims is excessive because the claims are drawn to a mucosal adjuvant that can be comprised of any IFN-α. The specification does not limit the type

or source of IFN-α that can be used in the claimed mucosal adjuvant. The specification, on p. 6-7, discloses that various types of natural IFN-α produced by macrophages or leukocytes, recombinant IFN-α produced in various cell types, as consensus IFN-α can constitute the "family of several interferons a" that can be used commensurate in scope with the claims of the instant application. The specification, on p. 7, also states that "although there are no special restrictions", any IFN-α that is safe for use in humans can be used. It is well-known in the art that the family of proteins known as IFN-α has multiple subtypes, and that some of the different IFN-α subtypes exhibit differences in biological activity (Pestka, *Biopolymers*, 2001, Vol. 55, p. 254-287 – see p. 254, 262, and Tables II and III). Additionally, it is also well-known in the art that the choice of host cell for producing recombinant proteins can affect the structure and function of the recombinant protein through the presence or absence of various post-translational modifications that can influence biological function. For instance, a recombinant IFN-α polypeptide produced by a prokaryotic host cell would not be glycosylated. Similarly, post-translation modifications such as sialylation are not universal among eukaryotic host cells; some insect, plant, and yeast host cells do not produce sialylated proteins (Sugyiami *et al*, 1993, *Eur. J. Biochem.*, Vol. 217, p. 921-927; Goochee *et al*, 1991, *Bio/Technology*, Vol. 9, p. 1347-1355; Krezdorn *et al*, 1994, *Eur. J. Biochem.*, Vol. 220, p. 809-817). Because the claims and the specification do not limit the type of IFN-α that can be used in the claimed mucosal adjuvant, the claims can be interpreted as reading on any IFN-α subtype, or from any source, and thus are drawn to IFN-α proteins which can differ in both structure and biological function.

Furthermore, the specification does not teach, or provide working examples of, any IFN-α other than the murine IFN-α of Examples 1-2, that can be used as a mucosal adjuvant. Because of the potential differences in biological function of different IFN-α subtypes, a person of ordinary skill in the art would not be able to predict if every IFN-α subtype, produced in any type of host cell, could be used as a mucosal adjuvant as claimed. Similarly, a person of ordinary skill in the art would not be able to predict if IFN-α from one species could be used in a mucosal adjuvant to vaccinate a different species. Such determinations would require undue experimentation on the part of the skilled artisan.

In summary, due to the excessive breadth of the claims, which read on the use of any IFN-α polypeptide from any source, the lack of guidance and examples in the specification that teaches any IFN-α except murine IFN-α, and the unpredictability of the art regarding the

different biological activities of different IFN-α subtypes, or IFNs produced in different host cells, a person of ordinary skill in the art would not be able to use any IFN-α except murine IFN-α, in a mucosal adjuvant without further, undue experimentation.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a vaccine composition comprising a vaccine antigen and IFN-α. As discussed above in the 35 U.S.C. 112, first paragraph, enablement rejection, the claims encompass any subtype of IFN-α, from any source, and from any species. Furthermore, as discussed above, the many possible IFN-α polypeptides can potentially differ in biological activity. The claims do not limit or define the IFN-α subtype(s) that can be used as an adjuvant as set forth in the claims, and therefore the Applicants have not fully described the genus of IFN-α polypeptides that can be used as an adjuvant in the claimed vaccine composition.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that the adjuvant comprise any IFN-α polypeptide, from any source or species. There is no identification of any particular subtype of IFN-α, other than the murine IFN-α of Examples 1-2, which can function as claimed. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus of IFN-α polypeptides useful as an adjuvant.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-8, 10-14, and 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Staats *et al* (WO 00/20028). The claims of the instant invention are drawn to a vaccine composition comprising a vaccine antigen, and IFN-α as an adjuvant, wherein said vaccine and IFN-α induces antigen-specific antibodies in both the blood and at mucosal surfaces when the vaccine-IFN-α is administered mucosally.

Staats *et al* teaches a method of eliciting an immune responseby administration of a vaccine antigen and an adjuvant (see abstract, and claim 1). Staats *et al* teaches that the vaccine antigen can be protein and peptide antigens, including protein/peptide antigens from a number of pathogenic organisms (see p. 21, line 11 – p. 23, line 2). Staats *et al* also teaches that the adjuvant can be a cytokine, and specifically teaches IFN-α as a cytokine that can be used (see p. 14, line 19 – p. 15, line 2, and claims 5-6). Furthermore, Staats *et al* teaches mucosal administration of the vaccine-adjuvant combination (claim 17), and also teaches that the vaccine-adjuvant induces both systemic (claim 22) and mucosal (claim 25) immune responses. Finally, by teaching that the vaccine and adjuvant are included together as a composition, Staats *et al* teach that the vaccine antigen and the adjuvant are administered at the same time and by the same route of administration.

Therefore, by teaching a vaccine-adjuvant composition comprised of any number of protein/peptide antigens and an adjuvant that can be IFN-α, wherein the vaccine-adjuvant composition is administered mucosally and stimulates systemic and mucosal immunity, Staats *et al* meets all limitations of claims 1-2, 4-8, 10-14, and 16-19 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 9, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staats et al (WO 00/20028). The claims of the instant invention are drawn to a vaccine composition comprising a vaccine antigen, and IFN-α as an adjuvant, wherein said vaccine and IFN-α induces antigen-specific antibodies in both the blood and at mucosal surfaces when the vaccine-IFN-α is administered mucosally. Claims 3, 9, and 15 of the instant application further state that the IFN-α in the vaccine composition is 0.5 to 5,000,000 IU.

Staats *et al* teaches a vaccine-adjuvant composition comprised of a protein/peptide antigen and an adjuvant that can be IFN-α, wherein the vaccine-adjuvant composition is administered mucosally at the same time, and wherein the vaccine-adjuvant composition induces systemic and mucosal immunity. Staats *et al* does not teach using 0.5 to 5,000,000 IU of IFN-α in the adjuvant. However, one of ordinary skill in the art, at the time the instant invention was made, would be motivated to follow the teachings of Staats *et al* and optimize the amount of IFN-α in order to produce a vaccine composition commensurate in scope with the claims of the instant invention. Such optimization would be within the abilities of a person of ordinary skill in the art, and would require nothing more than routine experimentation, thus giving the skilled artisan a reasonable expectation of success. Furthermore, it is noted that the claimed dose range of IFN-α is an exceedingly large, 10,000,000-fold range, and it is highly likely that any effective dose of IFN-α would fall within this range.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BDH
Art Unit 1646

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